

Remarks

Claims 1-8 and 32-43 are pending in this application. No amendments are made in this paper. No new matter has been introduced. Applicants respectfully submit that the pending claims are allowable for at least the following reasons.

A. The Rejection Under 35 U.S.C. § 103 Should Be Withdrawn

On pages 2-4 of the Office Action, claims 1-8 and 32-43 are rejected under 35 U.S.C. § 103, as allegedly obvious over Jeffery *et al.*, *J. Chem. Soc., Perkin Trans.*, 1: 2583-9 (1996) (“Jeffery”), U.S. Patent No. 6,331,571 to Jerussi *et al.* (“Jerussi”), and Fang *et al.*, *Tetrahedron: Asymmetry*, 10: 4477-4480 (1999) (“Fang”). In particular, in the Office Action, the Examiner alleges that the claims are obvious because: (1) Jeffery discloses compounds structurally similar to the claimed compounds, and Compound 5 in Jeffery “suggest stereoisomerisms similar to claimed herein”; (2) Jerussi also discloses structurally similar compounds and their stereoisomers; and (3) Fang discloses preparation of enantiomerically pure sibutramine and its metabolites, and based on the foregoing, the Examiner asserts that presently pending claims are obvious. Office Action, pages 2-3. Applicants respectfully traverse this rejection.

Three criteria must be met to establish a *prima facie* case of obviousness: 1) the prior art references must teach or suggest all the claim limitations; 2) there must be some suggestion or motivation to modify or combine the cited references; and 3) there must have been, at the time of the invention, a reasonable expectation of success. Manual of Patent Examining Procedure, § 2143.

First, Applicants respectfully point out that Jerussi cannot form a basis for a rejection under § 103 with regard to this application. The priority date of this application is November 30, 2000. Jerussi issued on December 18, 2001. As such, Jerussi is a § 102(e) reference. In this regard, Applicants respectfully point out that this application and Jerussi were commonly owned by Sepracor Inc. at the time of filing of this application. Consequently, Applicants respectfully request that Jerussi be removed from the combination of references cited in the Office Action. *See* 35 U.S.C. § 103(c).

Second, Applicants respectfully submit that the claims are not obvious over Jeffery and Fang because the three criteria required for a *prima facie* case of obviousness are not satisfied. As Applicants pointed out in their previous response,

Jeffery fails to meet all of the limitations of the pending claims because it does not disclose the stereoisomers of the claimed compounds. In response, the Examiner alleges that stereoisomerism of the claimed compounds is suggested by Jeffery, pointing to Compound 5a of Jeffery. Office Action, page 3. But as Applicants previously pointed out, while Compound 5a shows cis/trans isomerism, it does not show stereoisomerism of the compound. Moreover, even if Compound 5a did show the stereoisomers of the compound, Jeffery does not disclose their preparation. In fact, Jeffery actually discourages preparation of such stereoisomers, as discussed below.

The Examiner additionally cites to Fang, apparently implying that Fang's disclosure of preparation of the enantiomers of sibutramine and its metabolite would somehow cure the deficiency of Jeffery.¹ But Applicants respectfully submit that Fang adds nothing to the substance of the rejection. This is because Fang merely discloses the enantiomers of sibutramine and desmethylsibutramine, none of which are encompassed by the pending claims. Furthermore, while Fang discloses the preparation of the enantiomers, it is silent as to their desirability. Therefore, Fang would not have provided those of ordinary skill in the art with any motivation modify Jeffery so as to obtain the stereoisomers recited by the pending claims.

The Examiner also alleges that the pending claims are obvious because the difference between the claimed compounds and those disclosed in Jeffery is the position of hydroxy substitution, and because positional isomers are *prima facie* obvious. Office Action, page 3 (citing *In re Norris*, 179 F.2d 970 (C.C.P.A. 1950)). Regardless of whether such statement is accurate or not, Applicants respectfully point out that the claimed compounds are not mere positional isomers of the compounds disclosed in Jeffery, but are instead stereoisomers of positional isomers. As Applicants previously pointed out, stereoisomers, much less stereoisomers of positional isomers, are not per se obvious over the racemic compounds. Consequently, Applicants respectfully request that the rejection of the claims under 35 U.S.C. § 103 be withdrawn.

Finally, Applicants again point out that Jeffery would not have provided those of ordinary skill in the art with a motivation to make and use compounds of structures 4 and 5a, much less the stereoisomers thereof. For example,

¹ As discussed above, Jerussi cannot form a basis for an obviousness rejection.

Jeffery reports that the pharmacological activity of sibutramine is “mediated predominantly by” two demethylated amines of sibutramine (compounds 2 and 3). In their previous response, Applicants pointed out that this statement clearly implies that other metabolites of sibutramine would contribute little to sibutramine’s activity, and thus would have discouraged those of ordinary skill in the art to make and use other metabolites of sibutramine, much less stereoisomers thereof.

In response, the Examiner alleges that Applicants’ argument “is of little if any probative value inasmuch as the reference teach structurally similar compounds and its enantiomers.” Office Action, page 3. First, Applicants expressly dispute the Examiner’s statement that Jeffery discloses the enantiomers of the compounds discussed therein, for the reasons set forth above. More important, Applicants respectfully point out that the Examiner’s statement is flatly contrary to well-established legal principles concerning the (non)obviousness of a compound structurally similar to a prior art compound.

As Applicants previously pointed out, it is well-settled that each obviousness determination should rest on its own facts. *See, e.g., In re Grabiak*, 769 F.2d 729, 731 (Fed. Cir. 1985) (“Generalization should be avoided insofar as specific chemical structures are alleged to be *prima facie* obvious one from another.”). Thus, *prima facie* obviousness of a claimed compound cannot be established if its assertion is based on nothing more than a structural similarity between the claimed compound and those in the prior art. *See, e.g., Yamanouchi Pharm. Co., Ltd. v. Danbury Pharmacal, Inc.*, 231 F.3d 1339, 1343 (Fed. Cir. 2000) (“a *prima facie* case of obviousness requires structural similarity between claimed and prior art subject matter ... where the prior art gives reason or motivation to make the claimed compositions.”) (emphasis added). In addition, courts have consistently held that a finding of *prima facie* obviousness must be based on a consideration of the *Graham* factors, *e.g.*, the scope and content of the prior art, the difference between the prior art and the claimed invention, and the level of ordinary skill in the art. *See, e.g., In re Mayne*, 104 F.3d 1339, 1341 (Fed. Cir. 1997) (stating that determination of facts as to the *Graham* factors are fundamental to the legal determination under 35 U.S.C. § 103).

The pending claims are not obvious because Jeffery provides no “reason or motivation to make the claimed” compounds. *Yamanuchi*, 231 F.3d at 1343. Indeed, Jeffery clearly implies that the claimed compounds contribute little to sibutramine’s activity, thereby discouraging those of ordinary skill in the art from

making and using the claimed compounds. Without providing any evidence or argument that refutes the well-established legal principle or Applicants' arguments, the Examiner merely concludes that such arguments have little value because Jeffery teaches compounds that are structurally similar to the claimed compounds.² Such a conclusory statement simply begs the question, and cannot form the basis for an obviousness rejection. *See In re Sang-Su Lee*, 277 F.3d 1338, 1343-4 (Fed. Cir. 2002). Consequently, Applicants respectfully request that the rejection of the claims under 35 U.S.C. § 103 be withdrawn.

Conclusion

For at least the foregoing reasons, Applicants respectfully submit that all of the pending claims are allowable, and request that rejections directed to the claims be withdrawn.

No fee is believed due for this submission. Should any additional fees be due for this submission or to avoid abandonment of the application, please charge such fees to Jones Day Deposit Account No. 503013.

Respectfully submitted,

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² Although the Examiner appears to imply that the disclosure in Jeffery indicating that the claimed compounds contribute little to sibutramine's activity is overridden by Fang's disclosure that sibutramine is pharmacologically active, Applicants point out that such disclosure is irrelevant to the patentability of the claimed compounds. *See* Office Action, page 4. Whether sibutramine itself is pharmacologically active or not is not an issue here.